PALMITIC ACID INDUCES ALTERATIONS IN THE NEUROPROTECTIVE INSULIN-LIKE GROWTH FACTOR (IGF) SYSTEM IN ASTROCYTES

S. Guerra Cantera [1,2,3], F. Díaz [1,3], M. Torrecilla Parra [1,2], L.M. Frago [1,2,3], J. Argente [1,2,3,4], J.A. Chowen[1,3,4]
[1]. Hospital Infantil Universitario Niño Jesús, Madrid (España)
[2]. Facultad de Medicina, Universidad Autónoma de Madrid (España)
[3]. Centro de Investigación Biomédica en Red de la Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Madrid (España)
[4]. Instituto IMDEA Alimentación, Madrid (España)

Amongst the many roles of astrocytes is the regulation of central nutrient availability. They transport and metabolize nutrients, regulating what reaches neurons and protecting them against imbalances. These functions are of special importance in proximity to neuronal circuits controlling energy homeostasis. Increased levels of saturated fatty acids, *e.g.,* palmitic acid (PA), can cause neuronal damage. As IGF1 is a neuroprotective factor, we hypothesized that the IGF1 system is involved in the astrocytic response to PA.
Hypothalamic astrocyte cultures from male (M) and female (F) Wistar rats were treated 24h with PA (0.25 mM), IGF1 (10 or 50 ng/ml) or both. Relative gene expression was measured by RT-qPCR.
At 24h PA induced higher DNA damage-inducible transcript 3 (M: $p<0.01$, F: $p<0.001$) and IL-6 (M: $p<0.001$) mRNA levels, indicative of Endoplasmic reticulum (ER) stress. Exogenous IGF1 did not block this response. PA down-regulated mRNA levels of IGF1 (M: $p<0.001$; F: $p<0.05$), IGF2 (M: $p<0.001$; F: $p<0.05$), IGF binding protein (IGFBP)2 (M: $p<0.01$; F: $p<0.01$), IGFBP3 (M: $p<0.001$; $p<0.01$) and IGFBP4 (M: $p<0.01$), but increased expression of pregnancy-associated plasma protein-A (PAPP-A; M: $p<0.01$; F: $p<0.05$), a protease that liberates IGFs from IGFBPs to become bioactive, and its inhibitor stanniocalcin-2 (STC-2; M: $p<0.05$; F: $p<0.05$). Preliminary data indicate that astrocytes are RE-stressed 4 h after PA treatment, with an increase in STC-2, but no change in IGF1 or PAPP-A mRNA levels. At 8 h, cell stress is enhanced, with increased levels of PAPP-A and IGF1 mRNA.
In conclusion, the IGF1 system in astrocytes is modified by PA, which could be involved in the ability of astrocytes to protect nearby neurons, as well as in neuroendocrine control. The early effect of PA suggests a protective response as PAPP-A and IGF1 levels are increased, but IGF1 expression later decreases. Regulation of this system requires further investigation.